

Attorney Docket No.: **ISPH-0625**
Inventors: **Brett P. Monia**
Serial No.: **10/057,550**
Filing Date: **January 25, 2002**
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Please replace the paragraph beginning on page 48, lines 1
with the following rewritten paragraph:

-- There are multiple B-raf transcripts. The two most prevalent transcripts were quantitated after oligonucleotide treatment. These transcripts run at approximately 8.5 kb (upper transcript) and 4.7 kb (lower transcript) under the gel conditions used. Both transcripts are translated into B-raf protein in cells. In the initial screen, A549 cells were treated with oligonucleotides at a concentration of 200 nM oligonucleotide for four hours in the presence of lipofectin. Results were normalized and expressed as a percent of control. In this initial screen, oligonucleotides giving a reduction of either B-raf mRNA transcript of approximately 30% or greater were considered active. According to this criterion, oligonucleotides 13722, 13724, 13726, 13727, 13728, 13730, 13732, 13733, 13736, 13739, 13740, 13741, 13742, 13743, 14135, 14136, 14138 and 14144 were found to be active. These sequences are therefore preferred. Of these, oligonucleotides 13727, 13730, 13740, 13741, 13743 and 14144 showed 40-50% inhibition of one or both B-raf transcripts in at least one assay. These sequences are therefore more preferred. In one of the two

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assays, ISIS 14144 (~~SEQ ID NO: 23~~ SEQ ID NO: 90) reduced levels of both transcripts by 50-60% and ISIS 13741 (~~SEQ ID NO: 22~~ SEQ ID NO: 89) reduced both transcripts by 65-70%. These two sequences are therefore highly preferred.--
